intervention letters on the recurrence of exceptions, multiple regression models were developed using prescriber-level mean time (in days) between exceptions. In addition, the effect on medical costs and utilization was measured for a subset of data using a pre-post design with a control group. Pre-post periods were defined as 120 days before and after the date of intervention letters dated between May 1 and August 31, 2003. Controls were selected by matching to intervention cases using the propensity score methods. Sensitivity analysis was performed using varying time windows and bootstrap samples. Outcomes related to PMPM inpatient admissions, emergency room visits, and physician office visits were analyzed. **RESULTS:** Of 51,214 prescribers who had two or more exceptions during the 23-month time period, 6233 (12%) were randomly selected to receive intervention letters (ranging from one to 19). Model coefficients indicated that the time to exception was longer by 6.5 days ($p < 0.001$) as prescribers received additional intervention letters, after adjusting for the number of exceptions, severity level, and average patient age. There were no significant differences in medication costs from pre to post time periods, or between groups (study vs. control). However, the study group had fewer PMPM inpatient admissions and emergency room visits. **CONCLUSIONS:** Retrospective drug utilization review processes can have a positive effect in delaying next exceptions for prescribers and reducing utilization of health care services.

RX4

A DYNAMIC MODEL OF BUDGET IMPACT ANALYSES

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OBJECTIVE: Budget impact analysis (BIA) evaluates financial impacts of new technologies; it provides valuable information to decision-makers with a budget concern. This study proposes a dynamic model to incorporate variations in patients mix and drug prices over time in BIA. **METHODS:** The dynamic model is an inhomogeneous Markov Chain model. It contains three Markov states categorized by whether a patient's illness was treated with a generic drug, an existing brand-name drug, or the new brand-name drug. At each cycle, the model modifies the patient cohort by accounting for newly diagnosed incident cases and exiting cases due to cure or death. Also considered is a possible difference in the preference of treatment selection between the current and newly diagnosed patients. We conducted BIA on a simulated data using the Bayesian approach and presented the results in a probabilistic plot similar to the cost-effectiveness acceptability curve. A case study comparing the budget impact of including versus excluding a new drug in a health plan was used to demonstrate our method. The case study assumes the perspective of a payer and a time frame of five years. **RESULTS:** Results based on the simulated data showed that adding the new drug to the plan is associated with a budget increase in the short run but would reduce the budget in the long run. The probability that including the new drug would increase in the budget by 10% is 9%, 26% in a one- and two-year study timeframe, and it becomes cost neutral in the five-year timeframe. **CONCLUSIONS:** The proposed model provides a powerful framework to examine the time-varying parameters in BIA and generates estimates that better reflect health care market in the real world.

ADHERENCE/COMPLIANCE

AC1

CAPTURING PATIENT-REPORTED COMPLIANCE DATA IN A NINE-COUNTRY PRODUCT REGISTRY USING MEMS CAP DEVICES

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OBJECTIVE: To capture patient compliance data on a prescribed concomitant medication of an international product registry. The data needed to be collected in an accurate, timely, non-burdensome, and cost-effective manner. **METHODS:** Several patient compliance measurement options were considered but not selected including: physician office surveys, telephone surveys, and proxy responses. We chose the Medication Electronic Monitoring Systems (MEMS), which is a standard plastic vial, and a cap for the vial that contains a microelectronic circuit that records times when the cap is opened and closed. MEMS bottles and caps were given to participating clinicians with specific instructions for distribution to registry participants. MEMS were to be filled with a full 6-month prescription of the concomitant medication and distributed to patients at discharge. Patients were to be instructed to complete the prescribed regimen and received instructions on the use and purpose of the MEMS. They also were to receive written instructions on returning the MEMS to their clinician after 6 months. The clinicians were to return the MEMS caps to a centralized data processing center in the United States for analysis. **RESULTS:** MEMS were distributed to 707 patients, by 43 physicians, in 9 countries on 6 continents. The cost of distribution (including devices and mailings) was approximately $100.00 per patient. Delays in receiving MEMS caps from patients in a timely manner were experienced, as were delays in receiving MEMS caps from sites. Of the 240 MEMS devices administered, 26% returned the cap for analysis and 24% of the MEMS caps yielded analyzable data. **CONCLUSION:** Compared to other methods of collecting compliance data on a large international scale, MEMS provided a non-burdensome manner for collecting data. However, the low return rate indicates that this process must be monitored closely to maximize results, minimize costs and to ensure that patient utilization does not vary.

AC2

COMPARING PATIENT-REPORTED MEDICATION COMPLIANCE WITH ELECTRONICALLY MONITORED MEDICATION COMPLIANCE IN A 12-MONTH INTERNATIONAL REGISTRY

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OBJECTIVE: This study compares two compliance measurements, a telephone patient-reported survey and the Medication Electronic Monitoring System (MEMS), for a 12-month international registry studying re-intervention rates for interventional cardiology. **METHODS:** Patients were prescribed a 6-month anti-platelet drug regimen upon discharge from the hospital. Drug was supplied to all patients in a MEMS bottle, which contained an electronic cap that recorded internally the date and time the bottle was opened. At the end of six months, patients were to return the empty bottle to their provider for analysis. Patients included in this study were also contacted via telephone quarterly to recall their medication compliance status. The agreement between the two methods was evaluated using the weighted Cohen's kappa statistic (Kw). **RESULTS:** Of the 778 patients enrolled in the registry, 707 were given MEMS devices, and of those patients, 642 have reached the 6-month endpoint. A total

of 136 patients returned their bottles and completed a telephone survey. At Month 3, 98.53% of patients reported via telephone that they continually took the drug; 0.74% had temporary interruptions of the drug; 0.74% discontinued the drug early. At Month 3, MEMS data for those patients reported 44.85% with continuous administration, 39.71% with temporary interruptions, 15.44% discontinued early. Kw at Month 3 was 0.036 (95% CI = –0.018, 0.091). At Month 6, 83.82% of patients reported via telephone that they completed taking the drug; 15.44% were still taking the drug; 0.74% discontinued the drug early. At Month 6, MEMS data for those patients reported 63.24% completed, 0.74% were still taking, 36.03% discontinued early. Kw at Month 6 was 0.069 (95% CI = –0.005, 0.144). **CONCLUSION:** Based on the kappa statistic, there was little agreement between the patient-reported and electronic methods of measuring compliance. Patients reported being much more compliant with their medication regimen than was reported by MEMS.

AC3

COMPARISION OF ADHERENCE TO ANTIHYPERTENSIVES IN A MANAGED CARE POPULATION

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OBJECTIVES: A previous study conducted by the authors indicated that calcium channel blockers, ACE inhibitors, beta blockers and diuretics were the four most commonly used therapeutic classes of antihypertensives in a commercial HMO population. The objective of this study was to compare adherence between these four classes of antihypertensives. **METHODS:** This study was a retrospective pharmacy claims database analysis. All members evaluated had a diagnosis of hypertension, received at least two prescriptions for an antihypertensive drug, and were continuously enrolled during the one-year study period. The average medication possession ratio (MPR) was used as a primary adherence indicator. An analysis of covariance was conducted to determine if differences in the mean MPR existed based on the antihypertensive therapeutic class. Previous research in this population indicated that age, units per day of the drug, number of concurrent medications and total days supply were significant predictors of adherence. These factors were for in this analysis. **RESULTS:** The average MPR was evaluated for 1637 members meeting the inclusion criteria. The average age of the members was 52.85 year and 53.63% were female. The mean (S.D.) MPR for the therapeutic classes were: ACE inhibitors 0.8626 (0.2370), beta-blockers 0.8534 (0.2288), calcium channel blockers 0.8770 (0.2078), diuretics 0.8291 (0.2705). The MPR were significantly higher in members on calcium channel blockers versus diuretics (mean difference = 0.0524, 95% CI = 0.0140–0.0907, $p < 0.005$) and ACE inhibitors versus diuretics (mean difference = 0.0473, 95% CI = 0.0139–0.0808, $p < 0.005$). There were no significant differences in adherence between the other classes of antihypertensives. **CONCLUSIONS:** After controlling for significant predictors of adherence, the MPR for members on calcium channel blockers and ACE inhibitors were significantly higher than for those patients on diuretics. These results may have implications for the effectiveness of different therapeutic classes of antihypertensives in blood pressure control.

AC4

CLINICAL AND ECONOMIC OUTCOMES OF NON-ADHERENCE TO HIGHLY ACTIVE ANTIRETROVIRAL THERAPY IN PATIENTS WITH HIV

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OBJECTIVE: The objective of this study was to quantify the clinical and economic effects of non-adherence with triple therapy in treatment-naïve HIV patients. **METHODS:** A Markov model was developed to project quality-adjusted life expectancy and direct medical costs for HIV patients (mean age = 37 years) on an initial regimen of highly active antiretroviral therapy (HAART) with efavirenz, lamivudine and extended release stavudine given once daily. Each month, patients faced a risk of transition to AIDS that was a function of viral load, CD4 count, and adherence to drug therapy. Patients were assumed to change to another triple-therapy regimen if their viral load was ≥ 400 copies/mL or if they transitioned to AIDS. After four regimens, patients followed the natural history of the disease. We compared clinical and economic outcomes for two adherence scenarios: "clinical trial" (representing ideal utilization observed in clinical trials) and "typical" (based on observational studies in actual practice). Costs were derived from the HIV/AIDS Costs and Services Utilization Survey and average wholesale drug prices. Future costs and QALYs were discounted 3%. **RESULTS:** Mean discounted quality-adjusted life expectancy was 8.6 and 10.0 QALYs under the typical and clinical trial adherence scenarios, respectively. Lifetime direct medical costs in the typical and trial scenarios were $295,000 and $336,000, respectively. Compared with typical adherence, clinical trial adherence conferred an average gain of 1.4 QALYs at an incremental cost of $29,000 per QALY gained. Up to $1650 per patient per year could be spent on an intervention to improve adherence from typical to trial levels, and the incremental cost-effectiveness of doing so would remain below $50,000 per QALY gained. **CONCLUSIONS:** Typical adherence with HAART reduces quality-adjusted life expectancy by 14% compared to adherence levels in clinical trials. Programs to improve adherence appear to be a highly cost-effective use of resources.

PHARMACOEPIDEMIOLOGY

PE1

ASSESSING EFFECTIVENESS IN THE PRESENCE OF TREATMENT SWITCHING: DATA FROM AN EFFECTIVENESS STUDY OF ANTIPSYCHOTICS

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OBJECTIVES: Information on the comparative effectiveness of different antipsychotic medications in a naturalistic setting is important for clinicians and other health care decision-makers. However, in long-term naturalistic studies, patients may remain on treatment, switch, augment, or even stop treatment at any time and for different reasons—making statements about the causal effects of treatments difficult. The objective of this research was to assess several analytic strategies for comparing treatment effectiveness in the presence of switching. **METHODS:** Using data from a recently completed 1-year, randomized, naturalistic, anti-psychotic cost-effectiveness trial for schizophrenia, three different analysis strategies were utilized to compare the effectiveness of treatments on schizophrenia symptom severity (measured by BPRS total score): intent-to-treat, sub-setting by